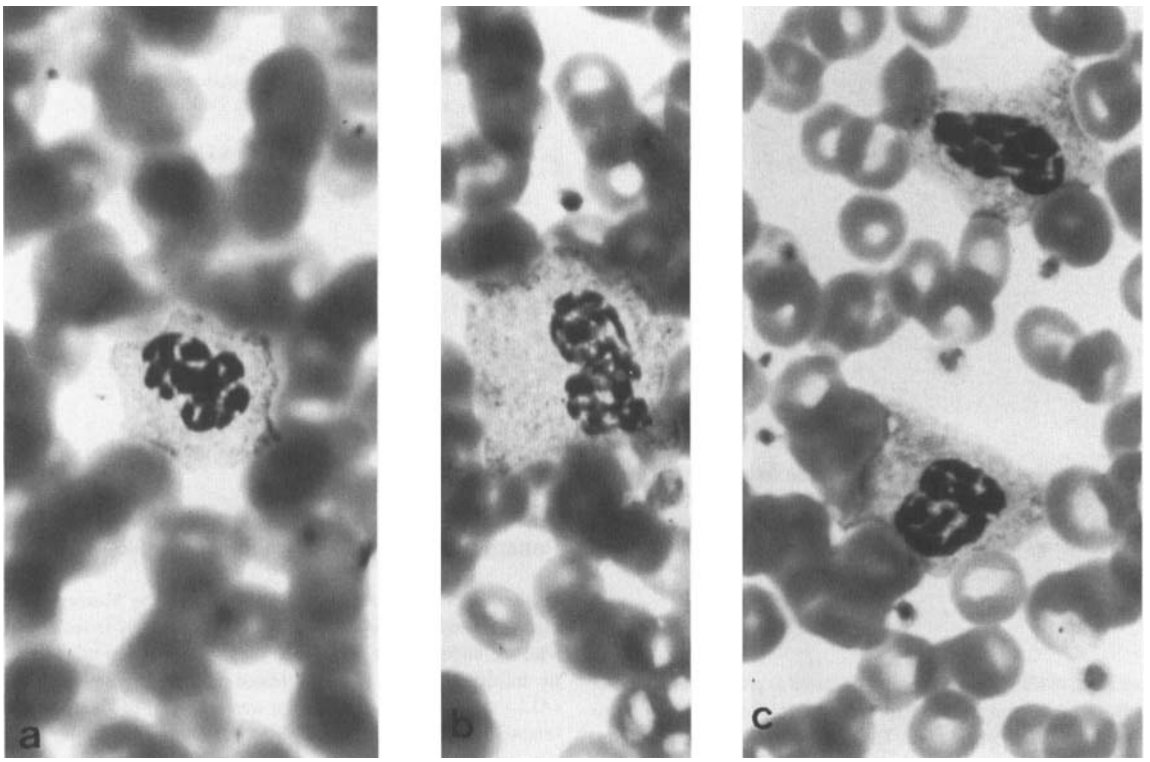

Fig. 1. Representative leukocytes from peripheral blood showing abnormal clumping chromatin. b: In a metamyelocyte. a and c: Associated with hyposegmentation in granulocytes. (May-Grünwald-Giemsa stain, ×1,200).

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Rearrangement of the *bcl*-6 Gene in Hodgkin's Disease, Lymphocyte Predominant Type

To the Editor: The *bcl*-6 gene encodes a protein belonging to the zinc-finger family, which regulates differentiation and development. A large study of 102 patients with large B-cell lymphoma revealed rearrangement of the *bcl*-6 gene in 20–25% of cases [1]. No such data exist for Hodgkin's disease. We report a case of Hodgkin's disease of the lymphocyte predominant type that was found to have a *bcl*-6 rearrangement.

A 53-year-old woman presented in January 1983 with enlarged lymph nodes over her left neck and a left breast mass. Biopsy studies of her lymph node and the left breast mass initially reported atypical lymphoid hyperplasia. Immunohistochemical study was inconclusive. She had persistent lymphadenopathy, and repeated lymph node biopsies in October 1983, October 1984, and August 1985 revealed a similar histology.

There was a progressive increase in the size of her left cervical lymph node by January 1987. Repeated lymph node biopsy revealed more definite features compatible with Hodgkin's disease, lymphocyte predominant, nodular type (LPHD). A review of all the biopsies showed a similar histological appearance, although the features were more typical in the later biopsies. The lymph nodes showed focal effacement of nodal architecture with replacement by nodular aggregates of lymphoid cells mainly composed of small lymphocytes; scattered L&H cells were identified. No typical Reed-Sternberg cells were found. The adjacent nodal tissue contained a few remnant follicles with some showing transformation of the germinal center. Immunohistochemical staining performed on paraffin sections showed that the L&H cells were positive for CD45 and the B-cell marker CD20 and negative for CD30, CD15, and the T-cell markers CD3 and CD45RO. The background small lymphocytes were composed of a mixture of B and T cells, with a predominance of the former. The features were in keeping with Hodgkin's disease, of the lymphocyte predominant, nodular subtype. Staging investigations found no evidence of disease dissemination. She received local radiotherapy, resulting in complete remission. She was last seen in March 1995, and there was no evidence of disease recurrence.

Frozen tissue obtained in 1987 was available for detection of *bcl*-6 gene rearrangement by Southern analysis. DNA was digested independently with *Bam*HI and *xba*I, and a 4-kb *Sac*-I-*Sac*-I fragment of the *bcl*-6 gene provided

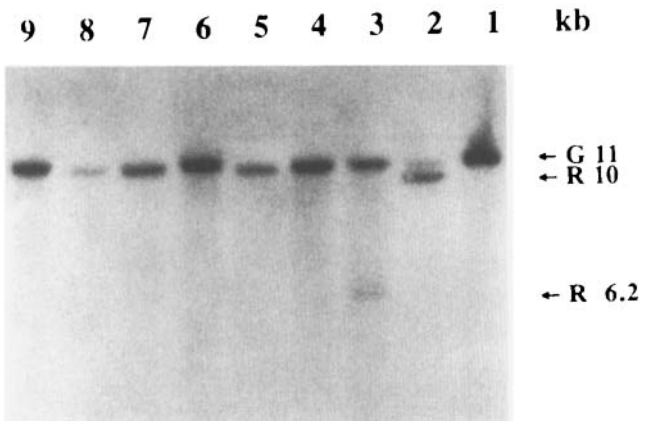

Fig. 1. Southern analysis using a *bcl*-6 probe following *Bam*HI digestion. Lane 1: Normal control. Lane 2: A case of diffuse large B-cell lymphoma with bcl-6 rearrangement. Lane 3: The case of LPHD reported here. Lanes 4–9: Other cases of lymphoma with no *bcl*-6 rearrangement.

by R. Dalla-Favera of Columbia University was used as probe [1]. Following *Bam*HI digestion, a rearranged band of 6.2 kb was found in addition to the 11-kb germline band (lane 3, Fig. 1). Also, following *xba*I digestion, a 5.6-kb rearranged band was seen in addition to the 13.5-kb germline band. They confirmed the presence of *bcl*-6 rearrangement in this case.

Many investigators have demonstrated B-cell-associated molecules in the L&H cells of LPHD. The tumor is considered to be of B-cell origin or to represent a large B-cell lymphoma in evolution [2–5]. Attempts have been made to demonstrate the clonality of LPHD. Techniques employed include Southern blot analysis and polymerase chain reaction (PCR) for detection of clonal immunoglobulin gene (Ig) rearrangement [2]. In situ analysis of immunoglobulin heavy chain protein or mRNA expression has also been used. Unfortunately, these methods have yielded conflicting results [5]. A new technique that isolated a single L&H cell for PCR detection of Ig gene heavy chain rearrangement has provided evidence for a B-cell origin but a polyclonal nature of the L&H cells [3].

This reported case has provided new insight into the biology of LPHD. The detection of a *bcl*-6 rearrangement in LPHD strongly suggests a clonal nature for LPHD and an intimate relationship between the tumor and non-Hodgkin's lymphoma of the diffuse large B-cell type. Further studies are necessary to define the incidence of *bcl*-6 gene rearrangement in LPHD and the precise relationship with large B-cell lymphoma.

Raymond Liang
Wing-Ping Chan

Department of Medicine,

Alexander C.L. Chan
Faith C.S. Ho

Department of Pathology, University of Hong Kong, Queen Mary Hospital, Hong Kong

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Two Cases of Epidemic Mucormycosis Infection in Patients With Acute Lymphoblastic Leukemia

To the Editor: Infection caused by fungus of the Mucorales order is uncommon and has been described almost exclusively in leukopenic patients who are undergoing chemotherapy [1]. We observed this rare opportunistic infection in two patients treated for acute lymphoblastic leukemia (ALL) at our institution. The first was a 40-year-old man with ALL2 who relapsed 11 months after completion of treatment. During the consolidation course of chemotherapy, febrile pneumopathy developed and bronchoalveolar lavage (BAL) identified *Xanthomonas maltophilia* associated with mucormycosis. Despite effective antibiotherapy against *Xanthomonas* and treatment with amphotericin B (Amb), the patient died of massive hemoptysis. Necropsy revealed rupture of the right auricle in the main right bronchus.

The second patient was a 35-year-old woman with a Ph1+ B ALL. During the aplasia induced by the consolidation treatment with high-dose cytosine-arabinoside plus amsacrine, the diagnosis of pulmonary filamentous mycosis was made on a BAL, and mucormycosis was identified on a liver biopsy done for two abscesses seen on echography. Stabilization of the hepatic lesion and 50% reduction of the pneumopathy was obtained by AmB and liposomal AmB. Three months later, while still in complete cytogenetic and molecular remission, she underwent pulmonary lobectomy and hepatic segmentectomy. Hepatic mucormycosis was confirmed, and mucormycosis was found associated with aspergillosis in the lung. Allogeneic bone marrow transplantation (BMT) was performed 2 months later for cytologic relapse. She died of extensive aspergillosis 90 day after BMT.

Mucormycosis is a rare fungal infection whose prognosis is almost always fatal in patients with acute leukemia [2]. One portal entry is the respiratory tract. The fungus can cause thrombosis, ischemia, and hemorrhage by erosion of the blood vessels. Early antimycotic therapy seems essential to improve the prognosis, but surgical resection of the infected tissue may be life saving.

Our two cases illustrate the risk of fatal hemoptysis associated with mucormycosis infection and the benefit of surgical resection recently reported by Pagano et al. [3]. Moreover, these cases point out several facts: 1) the two patients had received high-dose corticosteroid therapy, which has been shown to enhance *Aspergillus* growth in vitro [4]; the association of *Mucor* and aspergillosis suggests that the same risk factors, (corticosteroids and immunosuppression) are required for both; 2) even though surgical treatment of mucor abscesses was efficient in the second patient, aspergillosis developed despite AmB, liposomal AmB, and itraconazole therapy after BMT; the feasibility of BMT in patients with apparently cured aspergillosis is thus in question [5]; and 3) the major point is the epidemic risk of mucormycosis infection. These two patients stayed successively in the same room during aplasia; systematic control of surfaces led us to discover *Mucor* organisms on the ventilation grating. To our knowledge, this is the first